58. (Amended) A preparation of replication defective recombinant retrovirus expressing human factor IX protein, wherein said recombinant retrovirus preparation is resistant to degradation by human complement and [is capable of inducing] induces long term systemic expression of human factor IX when administered intravenously to a human afflicted with hemophilia B, wherein said long term systemic expression results in a measurable level of recombinant human factor IX protein being produced in the blood of said human for a period of at least 30 days after the administration of said recombinant retroviral vector preparation.

61. (Amended) A preparation of replication defective recombinant retrovirus expressing a therapeutic protein, wherein said recombinant retrovirus preparation is resistant to degradation by human complement and [is capable of inducing] induces long term systemic expression of said therapeutic protein when administered intravenously to a human, wherein said long term systemic expression results in a measurable level said therapeutic protein being produced in the blood of said human for a period of at least 30 days after the administration of said recombinant retroviral vector preparation.

REMARKS

Reconsideration of the application in view of the above amendments and following remarks is respectfully requested. Claims 1-11, 37-58 and 61-68 are presently pending in this application. Claims 1, 6,57, 58 and 61 have been amended for purpose of clarity. No new matter has been entered by these claims.

SEQUENCE LISTING

The Examiner has noted that the above-identified application fails to comply with the requirements set forth in 37 C.F.R. §§ 1.821-1.825. Accordingly, please find enclosed a new electronic and paper copy of the Sequence Listing that include no new material and are identical. Applicants respectfully submit that the above-identified application is now in compliance with 37 C.F.R. §§ 1.821-1.825 and WIPO Standard 25.

REJECTIONS UNDER 35 U.S.C. §112

Claims 6-11, 58 and 61-58 were rejected by the Examiner under 35 U.S.C. §112, first paragraph. In particular, the Examiner, citing *In re Wands*, asserted that the specification failed to teach one of skill in the art how to make and/or use the invention. The Examiner specifically asserted that no indication was made as to what particular methods lead to long term systemic expression of a therapeutic protein, and that no correlation was made between the disclosed animal model results and the ability for these results to be obtained in humans.

Applicants respectfully traverse this ground of rejection. Briefly, Applicants respectfully submit that with respect to enablement, nothing more than objective enablement is required in order to meet the requirements of 35 U.S.C. § 112(1). In particular, as stated by the Court of Customs and Patent Appeals:

> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. *In re Marzocchi* 169 USPQ 367, 369 (C.C.P.A. 1971) (emphasis original)

In the instant case, as noted by the Examiner Applicants have indeed shown that the subject invention can be utilized to produce expression of the factor VIII protein in the blood. The Examiner however suggests that since "only 3 out of the 6 examples showed expression of the protein at any time for at least 30 consecutive days", that the claimed invention is not enabled. Applicants respectfully disagree. In particular, the animal models show that statistically significant long-term expression can be achieved. To the extent the Examiner asserts that such expression can not be correlated to expression in humans, the Examiner is respectfully encouraged to provide Applicants with evidence that the animal models provided are not indicative of utility in humans.

Hence, absent specific objective evidence to the contrary, Applicants respectfully submit that the claimed subject is indeed enabled, and that the rejection of claims 6-11, 58 and 61-58 under 35 U.S.C. §112, first paragraph, has been traversed.

The Examiner also rejected claims 1-11, 57, 58 and 61 under 35 U.S.C. §112, second paragraph, for asserted failing to particularly point out and distinctly claim the subject matter of the present invention. More specifically, the Examiner objected to the phrase "capable of infecting" in claims 1 and 57, and "capable of inducing long term expression" in claims 6, 58 and 61. As noted above, applicants have amended these claims for purpose merely of clarity.

Hence, Applicants respectfully submit that the rejection of claims 1-11, 57, 58 and 61 under 35 U.S.C. §112, second paragraph, has been obviated.

REJECTION UNDER 35 U.S.C. §103

The Examiner also rejected claims 1-3 under 35 U.S.C. §103, as being unpatenable over Mulligan et al., in view of either Mason et al. or Takeuchi et al. In particular, the Examiner asserts that Mulligan et al. discloses a retrovirus encoding FVIII, and the production of retroviral particles from amphotrophic packaging cell lines.

Applicants respectfully traverse this ground of rejection. Briefly, where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under §103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 20 USPQ.2d 1438 (Fed. Cir. 1991)

In the instant case, the cited references do not provide to one of skill in the art a reasonable expectation of success to arrive at Applicants' claimed invention. In particular, while it might be obvious to try and produce complement-resistant retrovirus particles, the cited references either alone or in combination do not provide to one of ordinary skill in the art a reasonable expectation of success in constructing complement-resistant retroviral particles capable of expression FVIII which can be utilized in an *in vivo* clinical setting.

Therefore, Applicants respectfully submit that the rejection of claims 1-3 under 35 U.S.C. §103 has been traversed.

The Examiner also rejected claim 57 under 35 U.S.C. §103, asserting that the combination of Kay et al., in view of either Mason et al. or Takeuchi et al. renders; the claim

obvious. Applicants respectfully disagree. In particular, as noted above for FVIII, the cited references do not provide to one of skill in the art a reasonable expectation of success for constructing complement-resistant retroviral particles capable of expression FIX which can be utilized in an *in vivo* clinical setting.

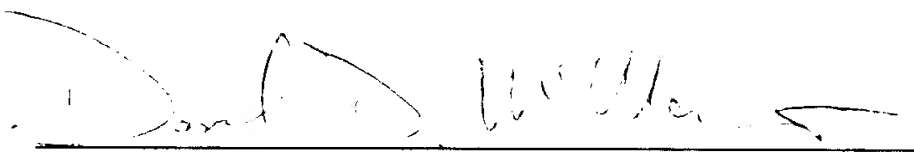
Therefore, Applicants respectfully submit that the rejection of claim 57 under 35 U.S.C. §103 has been traversed.

Based upon the above amendments and remarks, Applicants respectfully submit that the pending claims are now in a condition for allowance. Should the Examiner have any further questions or concerns, he is respectfully encouraged to contact the undersigned attorney at (206)-622-4900.

Respectfully submitted,

Douglas J. Jolly et al.

Seed Intellectual Property Law Group PLLC



David D. McMasters
Registration No. 33,963

DDM:lmn

Enclosures:

Check
Form PTO-1083 (+ copy)
Declaration re Sequence Listing;
Diskette containing Sequence Listing
Paper Copy of Sequence Listing
Petition for an Extension of Time (+ 2 copies)

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

wpn\ddm\930049\441C4-amendment